Notice of Allowability	Application No. 10/674,636	Applicant(s) CURTIS ET AL.	
	Examiner Sheridan L. Swope	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *December 19, 2005*.

2. ☒ The allowed claim(s) is/are *23-26 and 29-32*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

Applicant's response, on December 19, 2005, to the First Action on the Merits of this case mailed August 19, 2005, is acknowledged. It is acknowledged that applicants have cancelled Claims 21, 22, and 27-28 and amended Claims 23 and 29-32. Claims 23-26 and 29-32 are pending and are hereby reconsidered.

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Specification

Replace page 9, lines 22-24, with the following:

–For general information regarding PFAM identifiers, PS prefix and PF prefix domain identification numbers, refer to Sonnhammer et al. (1997) Protein 28:405-420.–

Replace page 10, line 25, to page 11, line 4, with the following:

–As used herein, the term "carboxylesterase domain" includes an amino acid sequence of about 300 to 650 amino acid residues in length and having a bit score for the alignment of the sequence to the carboxylesterase domain (HMM) of at least 300. Preferably, a carboxylesterase domain includes at least about 400-600 amino acids, more preferably about 450-550 amino acid residues, or about 490-510 amino acids and has a bit score for the alignment of the sequence to the carboxylesterase domain (HMM) of at least 400, 450, 500, 540 or greater. The carboxylesterase domain (HMM) has been assigned the PFAM Accession Number PF00135. An alignment of the carboxylesterase domain (amino acids 44 to 545 of SEQ ID NO:2) of human

53010 with a consensus amino acid sequence (SEQ ID NO:4) derived from a hidden Markov model is depicted in FIG. 2.–

Replace page 11, lines 10-25, with the following:

–To identify the presence of a "carboxylesterase" domain in a 53010 protein sequence, and make the determination that a polypeptide or protein of interest has a particular profile, the amino acid sequence of the protein can be searched against the Pfam database of HMMs (e.g., the Pfam database, release 2.1) using the default parameters. For example, the hmmsf program, which is available as part of the HMMER package of search programs, is a family specific default program for MILPAT0063 and a score of 15 is the default threshold score for determining a hit. Alternatively, the threshold score for determining a hit can be lowered (e.g., to 8 bits). A description of the Pfam database can be found in Sonhammer et al. (1997) Proteins 28(3):405-420 and a detailed description of HMMs can be found, for example, in Gribskov et al.(1990) Meth. Enzymol. 183:146-159; Gribskov et al. (1987) Proc. Nati. Acad. Sci. USA 84:4355-4358; Krogh et al.(1994) J. Mol. Biol. 235:1501-1531; and Stultz et al. (1993) Protein Sci. 2:305-314, the contents of which are incorporated herein by reference. A search was performed against the HMM database resulting in the identification of a "carboxylesterase" domain in the amino acid sequence of human 53010 at about residues 44 to 545 of SEQ ID NO:2 (see FIG. 2).–

Replace page 21, lines 10-23, with the following:

–The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch ((1970) J. Mol. Biol. 48:444-453) algorithm which has been incorporated into the GAP

program in the GCG software package, using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package, using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A particularly preferred set of parameters (and the one that should be used unless otherwise specified) are a Blossum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.–

Replace page 21, line 28, to page 22, line 9, with the following:

– The nucleic acid and protein sequences described herein can be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, et al. (1990) J. Mol. Biol. 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score=100, wordlength=12 to obtain nucleotide sequences homologous to 53010 nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score=50, wordlength=3 to obtain amino acid sequences homologous to 53010 protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., (1997) Nucleic Acids Res. 25:3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used.–

Claims

For Claim 23, line 3, replace –polypeptide– with –amino acid sequence–.

Authorization for this examiner's amendment was given in a telephone interview with Mario Cloutier on March 15, 2006.

Allowable Subject Matter

Claims 23-26 and 29-32 are allowed.

The following is an examiner's statement of reasons for allowance:

All elected Claims, 23-26 and 29-32, are limited to isolated polypeptides comprising the amino acid sequence of SEQ ID NO: 2 or variants of SEQ ID NO: 2 having carboxylesterase activity. The utility of the polypeptide of SEQ ID NO: 2 as having carboxylesterase activty is credible based on the following. The polypeptide of SEQ ID NO: 2 has the conserved catalytic Ser^{216}-Glu^{335}-His^{444} triad as well as the Glu^{127}-Asp-Cys-Leu-Tyr^{129} disulfide-bridge forming motif of carboxylesterases (see Satoh et al, 1998; pg 272-275). Based on the following evidence, a person of ordinary skill in the art would believe that, more likely than not, the polypeptide of SEQ ID NO: 2 has the same function as a polypeptide taught by Miyazaki et al, 2003. The polypeptide of SEQ ID NO: 2 has 65% homology, over the full-length, and 72% identity, within the catalytic domain, with the carboxylesterase of Miyazaki et al, 2003 (see enclosed alignments). Furthermore, both polypeptides are ~60kDa and both are highly expressed in kidney and brain (Miyazaki et al; pg 109, parg 2 and Fig 5). The polypeptide of Miyazaki et al is able to cleave the standard artificial carboxylesterase substrate p-nitrophenylacetate (Fig 4) and, thus, a person of ordinary skill in the art would believe that the polypeptide of SEQ ID NO: 2 would use p-nitrophenylacetate as a substrate. Carboxylesterases are known to cleave structurally diverse drugs and toxins (Satoh et al, 1998; pg 257). The ability of the polypeptide

of SEQ ID NO: 2 to cleave p-nitrophenylacetate provides a real-world use for said polypeptide in the screening for antagonists and inhibitors of carboxylesterases.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheridan Lee Swope, Ph.D.
Art Unit 1656

SHERIDAN SWOPE, PH.D.
PRIMARY EXAMINER